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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/798,119 | 03/11/2004 | Yih-Lin Chung | 13206-004002 / 0668-A2034 | 8809 |

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| EXAMINER | |
|---|---|
| HUGHES, ALICIA R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1614 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 03/23/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/798,119 | CHUNG, YIH-LIN | |
| | Examiner | Art Unit | |
| | Alicia R. Hughes | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-10,12,13 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,11 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *(1 page)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

Claims 1, 5, 11, and 14-17 are pending and the subject of this Office Action. Claims 2-4, 6-10, 12, 13, and 18-21 are withdrawn from consideration, being drawn to a non-elected invention. See 37 C.F.R. 1.142(b).

### *Restriction Requirement*

Applicant's election without traverse of claims 1, 5, 11, and 14-17, in the reply filed on 20 February 2007 is acknowledged. Upon reconsideration of the elections required previously, the Office hereby withdraws the requirement that Applicant elect a pharmaceutical carrier.

### *Claim Rejections - 35 U.S.C. §112.1*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 11, and 14-16 are rejected under 35 U.S.C. 112, first paragraph, because no mechanism of action or data is provided to support Applicant's claim for "increased therapeutic gained [measured] with low frequency of sequelae of therapy." Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. As a result, the

effect of performing the invention by one skilled in the art would be that of undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that the level of skill in cancer research is high, and the results of experiments to determine cancer recurrence or the lack thereof is unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Although the applicant has provided some working examples to support increased therapeutic gain in radiotherapy based on tumor control, the applicant has failed to disclose **any** examples or data to support a low frequency of sequelae of therapy for cancer as a result of treatment with a hyperacetylating agent.

While arguably, one of skill in the art, such as a physician or biomedical researcher with a master's degree or Ph.D. in the natural sciences, would be able to deduce results as to whether **a** treatment would result in increased therapeutic gain, the status in the art regarding whether a low frequency in the sequelae of therapy is so uncertain, because today, the causative effects of cancer is so controversial and the results so lacking in predictability, a conclusion about whether

the frequency of the sequelae of therapy would be low would be speculative, at best. *See generally*, Danesi, Romano et al., "Pharmacogenetic Determinants of Anti-Cancer Drug Activity and Toxicity," *TRENDS in Pharmacological Sciences*, Vol. 22, No. 8, pages 420-426 and page 420, the abstract, particularly (August 2001). In consideration of the foregoing, the art of the claimed invention lacks predictability because the claim is drawn too broadly.

***Claim Rejections – 35 U.S.C. §103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 11, and 14-16 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"].

Samid et al. teach new approaches to the "treatment of human malignancies such as advanced prostatic cancer, melanoma, brain tumors, and others" (Col. 2, lines 35-38), including a method for treating cancerous conditions with phenylacetic acid and its pharmaceutically acceptable salts and derivatives, including sodium phenylbutyrate (Col. 2, lines 64-67; col. 4, lines 61-67; col. 5, lines 1-15; col. 7, lines 1-4; col. 7, lines 55-57), and as well, cancer prevention (Col. 11, lines 36-47). Samid et al also teach a method of treating the cancer with sodium phenylbutyrate concomitantly or in combination with conventional radiotherapy (Col. 7, lines 47-51).

"The compounds of the present invention can be administered intravenously, enterally, parentally, intramuscularly, intranasally, subcutaneously, topically or orally" (Col. 3, lines 42-44). The dosage level of sodium phenylbutyrate administered ranges from 50 mg/kg/day to 1000 mg/kg/day (Col. 7, lines 14-21). Samid et al also teach that suitable formulations may include: soft gelatin capsules, dragees, pills, tablets, elixirs, suspensions, syrups, inhalations, rectal suppositories, implants, creams, gels, jellies, mucilages, pastes, ointments, infusion solutions, or nasal inhalations or sprays (Col. 24, lines 4-18).

Absent any express evidence to the contrary, in light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to administer sodium phenylbutyrate in the manner prescribed by Samid, in combination with radiotherapy, as a method of treating various cancers.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,877,213 [hereinafter referred to as "Samid"] in view of Shufeng, Z., et al., *5,6-Dimethylxanthenone-4-acetic acid (DMXAA): A New Biological Response Modifier for Cancer Therapy*, Investigational New Drugs, vol. 20, 2002, pages 281-295 [hereinafter referred to as "Shufeng, et al."].

The teachings of Samid, taught *supra*, are incorporated herein by reference. Samid also teach that sodium phenylbutyrate may be administered in combination with an antitumor agent or biological response modifier (Col. 7, lines 30-33 and col. 27, lines 59-60) as a method of treating various cancers.

Shufeng et al teach 5,6-dimethylxanthenone-4-acetic acid (DMXAA) as an investigational anti-cancer drug and as a biological response modifier (Summary, page 281, lines

1 and 31-32). Shufeng et al also teach that while DMXAA alone does not show "striking anti-tumor activity ... preclinical studies of DMXAA-drug combinations indicate that DMXAA may have a potential role in cancer treatment when co-administered with other drugs" (Page 281, lines 31-34 and page 282, lines 1).

One of ordinary skill in the art would be motivated to combine the teachings of Samid with the teachings of Shufeng et al., because the references teach overlapping subject matter, most notably, the treatment of cancer with anti-cancer/anti-tumor agents.

In light of the foregoing, one of ordinary skill in the art would be motivated to apply the teachings of Samid and the teachings of Shufeng et al to the present invention, because DMXAA is an anti-cancer agent/biological response modifier that when combined with radiotherapy and/or phenylacetic acid and its pharmaceutically acceptable salts and derivatives, including sodium phenylbutyrate, effectively treats various cancers. When used together, absent any express evidence to the contrary, in light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art that the proliferation of cancers and their associated tumors would be treatable through the combination therapy of sodium phenylbutyrate and DMXAA with radiotherapy.

## *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 A.M. until 5:00 P.M. on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application is proceeding is assigned 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

17 March 2007
ARH

Ardin H. Marschel 3/19/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER